REMARKS

Applicants have amended claims 1, 5, 7, 22, and 25. Support for amended claim 1 can be found, e.g., at page 8, line 28 through page 9, line 16 of the specification. Claims 5, 7, 22, and 25 have been amended to recite proper Markush group language. No new matter has been introduced by the amendment. Thus, the amendment should be entered as it raises no new issues that requires further consideration or search and also does not touch the merits of the application within the meaning of 37 C.F.R. § 1.116(b).

Claims 1-7, 9-11, and 21-31 are now pending. Reconsideration of the application, as amended, is requested in view of the following remarks.

Rejection under 35 U.S.C. § 102(b)

Claims 1, 4, 5, 7, 9, and 10 stand rejected as being anticipated by Lucas et al. (Wound Repair and Regeneration (1995) 3: 449-460; "Lucas"). See the Office Action, page 3, part 5.

Without acquiescing in the rejection, Applicants have amended claim 1 such that it now recites a limitation (i.e., isolating the mesenchymal stem cells prior to cell adherence to the culture device) clearly not disclosed or suggested by Lucas. Lucas describes separation of mesenchymal stem cells from myotubes after the cells have been plated, cultured, and released with trypsin (i.e, after the cells have adhered to the plate). See, e.g., the paragraph bringing page 450, right column and page 451, left column. As such, Lucas fails to teach all limitations recited in claim 1, and, therefore, does not anticipate claim 1.

For the amendment and reasons set forth above, Applicants submit that claim 1 is novel over the cited art. By the same token, claims 4, 5, 7, 9, and 10, all of which depend from claim 1, are also novel over the cited art.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1, 4-7, 9-11, and 30 as being unpatentable over Lucas in view of Bruder et al. (U.S. Patent No. 5,942,225; "Bruder"). See the Office Action, pages 3-4, part 6.

As mentioned above, amended claim 1 is drawn to a method for recovering mesenchymal stem cells which involves isolating mesenchymal stem cells prior to cell adherence to the culture device.

The primary reference, Lucas, describes separation of mesenchymal stem cells from myotubes after the cells have adhered to a culture plate. The secondary reference, Bruder, describes use of DMEM-LG medium for selective attachment of mesenchymal stem cells to a Petri dish. See, e.g., column 6, lines 44-57. As neither Lucas nor Bruder discloses or suggests isolating mesenchymal stem cells prior to cell adherence to the culture device, these two references, alone or combined, do not teach the method of claim 1.

For the reasons set forth above, claim 1, as amended, is patentably distinguishable over the cited art. By the same token, claims 4-7, 9-11, and 30, all of which depend from claim 1, are also distinguishable over the cited art.

NEW GROUNDS OF REJECTION

The Examiner further rejected claims 1-7, 9-11, and 21-31 on three new grounds, each of which is discussed below:

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1-7, 9-11, and 21-31 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appicants regard as the invention. Specifically, the Examiner pointed out that (1) claim 1 lacks a step referring back to the preamble, and (2) claim 25 recites improper Markush group language. See the Office Action, page 4, part 8. Applicants have overcome this rejection by amending claims 1 and 25 as shown above. The rejection should be withdrawn.

Rejection under 35 U.S.C. § 102(b)

The Examiner further rejected claims 1-5, 7, 9, 21, 22, 25, and 27 as being anticipated by Rieser et al. (U.S. Patent No. 6,242,247 B1; "Rieser"). See the Office Action, page 5, part 10.

As mentioned above, claim 1 has been amended to recite a step of "recovering the mesenchymal stem cells." As correctly pointed by the Examiner, Rieser does not teach such a

step. Thus, the method of claim 1 is not anticipated by Rieser. By the same token, claims 2-5, 7, 9, 21, 22, 25, and 27, all of which depend from claim 1, are also not anticipated by Rieser.

For the amendment and reasons set forth above, Applicants submit that claims 1-5, 7, 9, 21, 22, 25, and 27 are novel over the cited art.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-7, 9, 11, 21, 22, 24-27, 29, and 30 as being unpatentable over Rieser in view of Bruder. See the Office Action, pages 6-7, part 13.

Claim 1, as amended, is drawn to a method for recovering mesenchymal stem cells. The method involves (a) providing a mixture comprising mesenchymal stem cells; (b) seeding the mixture into a culture device and isolating the mesenchymal stem cells prior to cell adherence to the culture device; and (c) recovering the mesenchymal stem cells.

The primary reference, Rieser, describes a method for producing an implant containing cartilage tissue. The method includes growing cells with a chondrogenic potential on a porous plate made of a bone substitute material. The cells settle on the plate and produce an extracellular cartilage matrix. The cartilage tissue grows into pores of the plate, thereby forming an implant consisting of a bone substitute plate and a cartilage layer covering the plate. The two implant parts are connected to each other in a positively engaged manner by being grown together. The implant is then used for repairing enchondral and osteochondral defects. See, e.g., Abstract; column 1, lines 8-14; and column 12, line 57 through column 13, line 12. Note that the cells used for practicing Rieser's method can be chondrocytes, mesenchymal stem cells or other mesenchymal cells that have been isolated before being seeded on the plate, or a mixture of different cells. See, e.g., column 5, lines 16-36. There is no indication in Rieser that, when a mixture of different cells (e.g., including mesenchymal stem cells and other cells) are used, the mesenchymal stem cells should be separated from the other cells either before or after seeding of the mixture on the plate, or the separated mesenchymal stem cells, if any, should be recovered. In contrast, Rieser states that "[i]t is not necessary to isolate specific cell types" (e.g., mesenchymal stem cells). Even if the mesenchymal stem cells accidentally separate themselves from the other cells inside the implant, such separated mesenchymal stem cells are not later recoved. Rather, the entire implant (i.e., including both the mesenchymal stem cells and the

other cells) is used to repair enchondral and osteochondral defects. Thus, Rieser teaches away from the method of claim 1 by discouraging an artisan from isolating mesenchymal stem cells after seeding a mixture of cells in a culture device and from recovering the isolated mesenchymal stem cells.

The secondary reference, Bruder, describes a method of separating and recovering mesenchymal stem cells based on selective attachment. For example, Bruder states:

> "The human mesenchymal stem cells isolated and purified as described here can be derived, for example, from bone marrow, blood, dermis or periosteum. When obtained from bone marrow this can be marrow from a number of different sources, including plugs of femoral head cancellous bone pieces, obtained from patients with degenerative joint disease during hip or knee replacement surgery, or from aspirated marrow obtained from normal donors and oncology patients who have marrow harvested for future bone marrow transplantation. The harvested marrow is then prepared for cell culture. The isolation process involves the use of a specially prepared medium that contains agents which allow for not only mesenchymal stem cell growth without differentiation, but also for the direct adherence of only the mesenchymal stem cells to the plastic or glass surface of the culture vessel. By creating a medium which allows for the selective attachment of the desired mesenchymal stem cells which were present in the mesenchymal tissue samples in very minute amounts, it then became possible to separate the mesenchymal stem cells from the other cells (i.e. red and white blood cells, other differentiated mesenchymal cells, etc.) present in the mesenchymal tissue of origin." (Column 4, lines 15-36; emphasis added)

Clearly, Bruder's method requires that separation of mesenchymal stem cells from other cells take place after the mesenchymal stem cells have attached to the culture vessel. This is contrary to the method of claim 1 which requires that separation of mesenchymal stem cells from other cells take place prior to the mesenchymal stem cells have attached to the culture vessel. Thus, Bruder also teaches away from the method of claim 1.

As both Rieser and Bruder teach away from the method of claim 1, neither of them, alone or combined, would have provided motivation for a skilled person in the art to combine the two references to come up with the method of claim 1. Applicants hence submit that claim 1, as amended, is unobvious over the cited art. By the same token, claims 2-7, 9, 11, 21, 22, 24-27, 29, and 30, all of which depend from claim 1, are also unobvious over the cited art.

CONCLUSION

Applicants submit that the grounds for rejection asserted by the Examiner have been overcome, and the claims, as pending, define subject matter that is novel, definite, and non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.